

### AMENDMENTS

Claims 1-13 are pending.

Claims 1, 4, 11, and 12 have been amended.

Claim 13 has been added.

Support for the amendments is found in the claims and specification, as originally filed. Support for claims 1 and 11 can be found in claim 4, page 6, page 10, first paragraph, page 12, page 14, and Example 1. Support for the limitation “a composition comprises (B) and does not comprises a phosphate ion supplying compound” can be found in Examples 1 and 2 of Table 1 on page 18 which show that the only source of a phosphate ion is a polyolphosphate ion supplying compound which is separated from a fluoride ion supplying compound other than a monofluorophosphate ion supplying compound. Composition Y comprising the fluoride ion supplying compound other than a monofluorophosphate ion supplying compound does not comprise a source of a phosphate ion.

No new matter is believed to have been added.

The purpose of the written description requirement is to ensure that a patent application conveys to a person of skill in the art that the applicants had possession of the claimed invention. See, e.g., *LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1731 (Fed. Cir. 2005). In *Ex parte Parks*, the Board stated that “a lack of literal support does not, in and of itself, establish a prima facie case of lack of adequate description support, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Int. 1993). Also, a disclosure need not recite the claimed invention *in haec verba*. *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 923 (Fed. Cir. 2004).

Thus, it is clear from the specification that the claimed oral preparation does not comprise a phosphate ion supplying component in the composition comprising a fluoride ion supplying compound other than a monofluorophosphate ion supplying compound.

REMARKS/ARGUMENTS

Applicants wish to thank the Examiner for a discussion on September 16, 2009. The rejections over Winston et al. and Ishihara et al. were discussed in view of the proposed amendments.

The present invention provides an oral preparation system which is able to form the primary particles of calcium fluoride and able to control the rate of calcium fluoride aggregation (namely, the formation of secondary particle) and, accordingly, allows greater adsorption of calcium fluoride fine particles on the teeth, thus being excellent in effects of inhibiting demineralization of the tooth and accelerating remineralization. See page 5 of the present specification.

The present inventors have found that polyolphosphate ions can control the particle size of the secondary particle of calcium fluoride (a calcium fluoride aggregate) by reducing the size of the primary particle of calcium fluoride to a smaller size and by inhibiting the primary particle aggregation (the formation of a secondary particle). See page 5 of the present specification.

Claims 1-12 are rejected under 35 U.S.C. 103(a) over Winston et al., US 5,817,296, or Ishihara et al., US 6,770,265. The rejection is traversed because the references do not describe or suggest:

(a) an oral preparation comprising two compositions, wherein (i) the components (A) and (B) are separated, and (ii) a second composition comprising (B) does not comprise a phosphate ion supplying compound;

(b) primary and secondary fluoride particles, as in claims 5 and 6;

(c) mixing a calcium compound (A) with a monofluorophosphate (D) followed by admixing a different fluoride compound (B) which is kept separately, and then incorporating a polyolphosphate compound (C) into the system, as in claim 12; and

(d) using two different sources of calcium in one composition, as in claim 13.

(e) The claimed composition provides an advantageous adsorption of fluoride compared to the preparations of the cited references, wherein an inorganic phosphate is added to the composition comprising fluoride.

Winston et al. describe a tooth treating composition comprising part I including a calcium salt and another divalent metal salt, and part II including a phosphate salt and, optionally, a fluoride agent (col. 4, lines 25-35). Upon mixing, the Winston et al. composition precipitates (col. 6). In part II, phosphate is an inorganic phosphate (col. 6, lines 60-67). Winston et al. describe various fluoride compounds including a monofluorophosphate (col. 8, lines 3-24; and the Examples). Winston et al. describe that a fluoride compound is included in part II with phosphate for better re-mineralization (col. 3, lines 34-40). Winston et al. also describe that when a monofluorophosphate is used, it can be added to part I with a calcium salt, but it is less desirable because of the potential loss of the fluoride (col. 8, lines 18-24).

The Examiner has alleged that part I can comprise calcium glycerophosphate as a calcium (A) source and a phosphate (C) source and a monofluorophosphate (D). However, Winston et al. do not describe also using a different fluoride compound in part II.

The Examiner is of the opinion that because the potential loss of fluoride when a monofluorophosphate is added to part I with a Ca salt, one would have been motivated to also add fluoride to part II to provide “enough” fluoride.

The Examiner’s assertion regarding “to ensure that enough fluoride was present” is not supported because the Examiner has not explained what “enough fluoride” means and for what purpose there should be “enough fluoride”. For example, Winston et al. describe that fluoride is *optional* and can be present in the amount from 0.01% to 10%. Thus, even when there is some or complete loss of a monofluorophosphate from part I, there is still “enough” fluoride to achieve the Winston et al. goal (i.e., remineralize or desensitize teeth by

an application a calcium salt and another divalent metal salt) because fluoride is *optional* or can present as low as 0.01%.

Further, Winston et al. describe using a fluoride compound in only one composition, i.e., in part I for any fluoride compound described in Winston et al. or in part II when the fluoride compound is monofluorophosphate. The Examples show that fluoride compounds including monofluorophosphate are only used in part II in combination with inorganic phosphates. Thus, Winston et al. do not describe or suggest using two different fluorides in different parts of the system.

Thus, although Winston et al. describe various fluoride compounds can be used, one would not have been motivated to use a monofluorophosphate in part I and another fluoride in part II because (i) Winston et al. explicitly describe separating calcium and fluoride compounds, (ii) discourage using a monofluorophosphate in part I, and (iii) suggest using fluoride compounds in part II with an inorganic phosphate which is not used in the claimed composition in which a source of phosphate ions is a polyolphosphate ion supplying compound separated from the fluoride ion.

Winston et al. do not describe forming primary and/or secondary calcium fluoride particles, as in claims 5 and 6. Since the oral composition of Winston et al. is different from that claimed, these properties are not inherent.

Ishihara et al. describe a tooth surface treatment system comprising two separate compositions that are mixed in the mouth (col. 2). One composition comprises a calcium salt and an acid, while the other composition comprises a phosphate other than a calcium salt. Using fluoride compounds is optional in the part comprising a phosphate (see col. 5, lines 5-24, Examples 4-5, 7, and claims 1, 3, and 4). Ishihara et al. describe various sources of a fluoride including a monofluorophosphate (col. 5, lines 15-23). Also, calcium may be calcium glycerophosphate (col. 4, lines 5-6).

Ishihara et al. do not describe using different fluorides in the first and second compositions. Thus, Ishihara et al. describe that when a calcium source is calcium glycerophosphate (as pointed by the Examiner), phosphates are not calcium salts. Ishihara et al. do not describe a non-calcium salt of glycerophosphate or another polyolphosphate. Ishihara et al. only describe using inorganic phosphates as a source of phosphate ions.

Thus, Ishihara et al. do not describe using (A) a calcium ion compound and (C) a polyolphosphate ion compound of claim 1 because Ishihara et al. describe that the phosphate is not a calcium salt, and the only polyolphosphate compound described in Ishihara et al. is calcium glycerophosphate which is a calcium salt.

In addition, the Examiner has alleged that it would have been obvious to use fluorides in both compositions because Ishihara et al. describe using various fluoride compounds. Applicants respectfully disagree.

It would not have been obvious to use different fluorides in both compositions because in Ishihara et al., using a fluoride compound even in one composition is optional. Further, the examiner has not provided any explanation of why one would have “desired” to use fluoride salts in both compositions and why one would have used different fluorides in two compositions (see page 6 of the Official Action).

Concerning claims 5 and 6, the compositions of the cited references are different (e.g., the prior art compositions include inorganic phosphates) and, therefore, the size of primary particles is not necessarily the same as claimed and a secondary particles are not necessarily formed.

Concerning claim 12, Winston et al. and Ishihara et al. do not describe mixing a calcium compound (A) with a monofluorophosphate (D) followed by admixing a different fluoride compound (B) which is kept separately, and then incorporating a polyolphosphate compound (C) into the system.

Concerning claim 13, Winston et al. and Ishihara et al. do not describe using two different sources of calcium in one composition, wherein one calcium source is calcium polyolphosphate.

Applicants conducted the following experiments showing that the amount of fluorine adsorption is extremely decreased by adding a phosphate compound (dipotassium phosphate) to the compound (B) which is a fluoride ion supplying compound other than a monofluorophosphate ion supplying compound.

The testing method is the same as the method disclosed in the Examples of the specification.

The HAP pellet was immersed alternatively three times in A and B agents of 10 ml each (total immersion time: 3 minutes). The immersion (treating) method is the same as the method disclosed in “b. Quantitative Determination of Amount of Fluorine Adsorption on HAP Pallet” of the specification.

The experiment was conducted at pH7.

The content of phosphoric acid in Comparative Example B1 is the same as that of the phosphate ion supplying compound in Example 6 of Winston.

In Comparative Example B2, a ratio of calcium ions to phosphate ions is made close to that of Example 6 in Winston.

In Comparative Example B3, the phosphate ion concentration is further lowered and gets closer to 1,000 ppm. The phosphate ion concentration in Winston et al. is 100 to 40,000 ppm, preferably 1,000 to 40,000 ppm (col. 6-7, the bridging paragraph). In Examples 5 and 6 of Winston et al., the content of phosphate compounds is 3.5 and 2.5 wt.%, respectively. In Examples 13 and 14, the content of phosphate compounds is 4.4 and 3.4 wt.%, respectively. Ishihara et al. describe that the content of a water-soluble phosphate is 2-30 wt.% (col. 4, ln. 46-48).

Further, Winston et al. describe the calcium ion content of 100-35,000 ppm, the fluoride compound content of 0.01-5.0 wt. %, and a pH of 4-7 (col. 4 and 6). Ishihara et al. describe the calcium salt content of 2-30 wt.%, the fluoride content of 0.0001-3 wt.%, and a pH of 2-7 (col. 2 and 6).

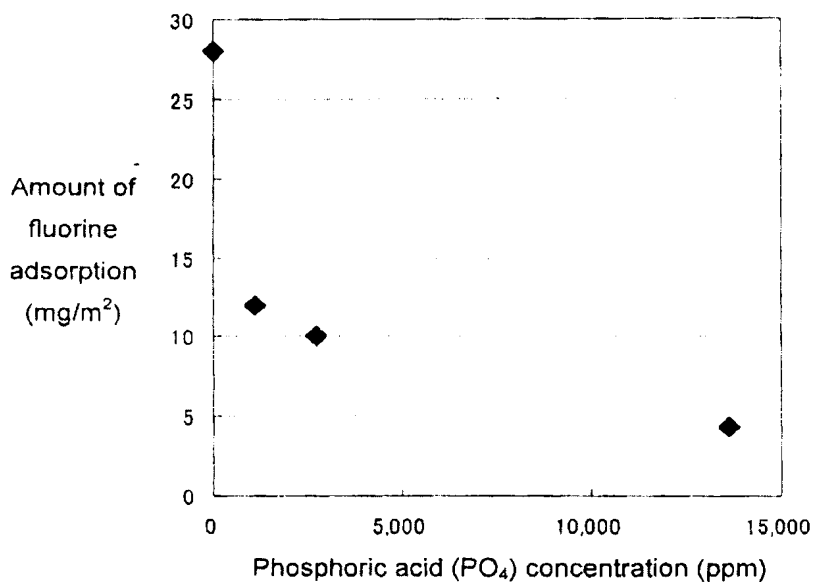
The comparative examples provided below show that the amount of adsorbed fluoride is decreased when an inorganic phosphate is added. The comparative example cover the range of the phosphate ion of the cited references, i.e., 1,090 ppm of Comparative Example B3; 2,727 ppm of Comparative Example B2; and 13,635 ppm of Comparative Example B1.

Component (wt%)	Example B1		Comparative Example B1		Comparative Example B2		Comparative Example B3	
	A	B	A	B	A	B	A	B
Calcium glycerophosphate	0.5	--	0.5	--	0.5	--	0.5	
Calcium lactate	0.5	--	0.5	--	0.5	--	0.5	
Sodium monofluorophosphate	0.7	--	0.7	--	0.7	--	0.7	
Sodium fluoride	--	0.2	--	0.2	--	0.2	--	0.2
<b>Dipotassium phosphate</b>	--	--	--	<b>2.5</b>	--	<b>0.5</b>	--	<b>0.2</b>
Purified water	Balance							
Total	100	100	100	100	100	100	100	100
Amount of fluorine adsorption (mg/m <sup>2</sup> )	<b>28</b>		<b>4.3</b>		<b>10</b>		<b>12</b>	
Phosphoric acid (PO <sub>4</sub> ) concentration (ppm)	--		13,635		2,727		1,090	
Phosphoric acid (PO <sub>4</sub> ) concentration (μmol/g)	--		440		88		35	

In the calculation of phosphoric acid concentration, 1L solution was regarded as 1 kg.  
 Calcium: About 40 μmol/g

It is clear from the results that the amount of fluorine adsorption is extremely decreased by adding a phosphate compound (dipotassium phosphate) to the compound (B).

The graph below shows the relationship between the phosphoric acid ( $\text{PO}_4$ ) concentration (ppm) and the amount of fluorine adsorption ( $\text{mg/m}^2$ ) based on the conducted experiments.



The claimed oral preparation provides an advantageous result which is not suggested by the cited references.

Thus, neither Winston et al. nor Ishihara et al. make the claimed oral composition obvious.

Applicants request that the rejection be withdrawn.

A Notice of Allowance for all pending claims is requested.

Respectfully submitted,

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